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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,498	01/09/2006	Xu Zhang	514572000600	7048
25225 7590 12/12/2007 MORRISON & FOERSTER LLP 12531 HIGH BLUFF DRIVE SUITE 100 SAN DIEGO, CA 92130-2040			EXAMINER SNYDER, STUART	
			ART UNIT 1648	PAPER NUMBER
			MAIL DATE 12/12/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/538,498

Applicant(s)

ZHANG ET AL.

Examiner

Stuart W. Snyder

Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 September 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 7, 8 and 10-56 is/are pending in the application.
- 4a) Of the above claim(s) 3, 4 and 34-55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-2, 7-8, 10-33 and 56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

1. Amendment of claims 1, 8, and 32, cancellation of claims 5, 6, and 9, and addition of new claim 56 is acknowledged in Applicants' filing of 9/26/2007. Claims 1, 2, 7-8, 10-33, and 56 are pending and examined herein; claims 3-4 and 34-55 were previously withdrawn as being drawn to non-elected inventions.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 23 and 32 were previously rejected as being indefinite because of the limitations "Eppendorf tubes" and "physiological salt water", respectively. Applicants' arguments and amendments have been carefully considered and the rejections are **WITHDRAWN**.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Rejection of claims 1-2, 5-9, 11, 13-15, 22, and 24-33 under 35 USC § 102 as being anticipated by Antoine, *et al.* is **WITHDRAWN** in view of Applicants' amendment of claim 1.

4. Claims 1, 2, 7, 10, 11, 13-17, 22-28, 31-33 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Janssen and Rios (1989). Claims 1, 2, 7, 10, 11, 13-17, 22-28, 31-33 and 56 are, *inter alia*, generally drawn to methods of cell, cellular organelle or virus separation using magnetic microbeads that have not been modified with moieties that specifically bind cells, viruses or cellular organelles comprising the steps of contacting samples suspected of containing such entities under conditions that would permit non-specific association and separating microbead/biological entity from the sample. Other claims add the following limitations: The target cell is selected from a group of specified cell types (claim 2), the nature of the metal (claim 7), the size of the microbead (claim 10), the nature of microbead modification (claim 11), the method includes a washing step (claims 13 and 17) having a pH of about 6.5 (claims 32 and 56), the method includes a recovery step (claim 14) that includes using magnetic force (claims 15 and 33), the sample is a clinical sample (claim 16) selected from specifically recited types (claim 17), the time of the method is between 1 and 20 min (claim 22), the method includes use of an eppendorf tube (claim 23), the method does not include a precipitation procedure (claim 24) or poisonous agent (claim 25), the method is conducted at room temperature (claim 26), and the method is used to isolate a leukocyte from fresh or low-temperature conserved (claim 28) whole blood, marrow or lymph (claim 27).
- Janssen and Rios teaches a method of preparation of leukocytes from patient fresh whole blood using paramagnetic, unmodified polystyrene microspheres

having an average diameter of ____ nm, includes a washing step with PBS having a pH of about ____, includes a cellular recovery step, involves magnetic separation in the washing and recovery steps; the procedure takes approximately 10-20 min, is performed at room temperature, and does not include precipitation steps or poisonous agents. Thus, Janssen and Rios teach each and every limitation of claims 1, 2, 7, 10, 11, 13-15, 22-28, 31-33 and 56.

5. Claims 1, 2, 7, 10, 11, 13-17, 22-26 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by Fletcher (1976). Claims 1, 2, 7, 10, 11, 13-17, and 22-26 are, *inter alia*, generally drawn to methods of cell, cellular organelle or virus separation using magnetic microbeads that have not been modified with moieties that specifically bind cells, viruses or cellular organelles comprising the steps of contacting samples suspected of containing such entities under conditions that would permit non-specific association and separating microbead/biological entity from the sample. Other claims add the following limitations: The target cell is selected from a group of specified cell types (claim 2), the nature of the metal (claims 7), the size of the microbead (claim 10), the nature of microbead modification (claim 11), the method includes a washing step (claims 13 and 17) having a pH of about 6.5 (claims 32 and 56), the method includes a recovery step (claim 14) that includes using magnetic force (claims 15 and 33), the time of the method is between 1 and 20 min (claim 22), the method includes use of an eppendorf tube (claim 23), the method does not include a precipitation procedure

(claim 24) or poisonous agent (claim 25), and the method is conducted at room temperature (claim 26).

Fletcher teaches a method of preparation of marine pseudomonads using paramagnetic (ferric oxide), unmodified polystyrene microspheres having an average diameter of ____ nm, includes a washing step with PBS having a pH of about ____, includes a cellular recovery step, involves magnetic separation in the washing and recovery steps; the procedure takes approximately 10-20 min, is performed at room temperature, and does not include precipitation steps or poisonous agents. Thus, Fletcher teaches each and every limitation of claims 1, 2, 7, 10, 11, 13-17, 22-26 and 56.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 10, 12, 16, 17, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Janssen and Rios as applied to claims 1, 2, 7, 10, 11, 13-17, 22-28, 31-33 and 56, or Fletcher as applied to claims 1, 2, 7, 10, 11, 13-17, 22-26 and 56, above and in further view of Ullman, *et al.* The claims are drawn to the method outlined above with the additional limitations: Microbead size between about 5×10^{-9} and 5×10^{-5} m, the microbead is modified to comprise a hydroxyl group, the sample selected from among various clinical

specimen types specifically including blood, and the method completed within about 1 min. to about 20 min. Janssen and Rios does not teach the aforementioned limitations. Ullman, *et al.* teaches use of a microbead sized between 2×10^{-8} and 1×10^{-4} m (a range that overlaps with the range of claim 10, see column 6, lines 65 ff), polymeric microbeads comprising hydroxyl groups (see column 7, lines 32 (alcohol) and 34 (free hydroxyl)), a clinical specimen (see, column 16, lines 62-64), a sample comprising blood (see column 13, lines 39-41), and the time of completing the method of 15-85 sec (this overlaps with the range of 1-10 min of claim 22; see column 18 lines 18-31 especially line 27).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Janssen and Rios by using the limitations described above as taught by Ullman, *et al.* The skilled artisan would have been motivated to do so because both methods have a common goal of isolating cells and it is inherently obvious to combine features of similar methods. There would have been a reasonable expectation of success, given the success of the method, as taught by Ullman, *et al.* (see, especially the Examples section of the Patent). Thus, the invention of claims 10, 12, 16, 17, and 22 was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

7. Claims 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Janssen and Rios as applied to claims 1, 2, 7, 10, 11, 13-17, 22-28, 31-33 and 56, or Fletcher as applied to claims 1, 2, 7, 10, 11, 13-17, 22-26 and 56,

above and in further view of Brinchmann, *et al.* Neither Janssen and Rios nor Fletcher teaches further separation of biological material, especially an oligonucleotide that is subsequently amplified using an automated procedure. Brinchmann, *et al.* teaches a method of separating HIV-infected cells from whole blood, washing the cell, isolating either HIV RNA or HIV DNA and amplifying the oligonucleotides (PCR of *pol* gene). Brinchmann, *et al.* does not specifically teach an automated procedure; however it is inherently obvious to automate a manual method (see MPEP 2144.04, quoted below).

In re Venner, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958) (Appellant argued that claims to a permanent mold casting apparatus for molding trunk pistons were allowable over the prior art because the claimed invention combined "old permanent-mold structures together with a timer and solenoid which automatically actuates the known pressure valve system to release the inner core after a predetermined time has elapsed." The court held that broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art.).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Janssen and Rios or Fletcher by using the limitation of the claims as taught by Brinchmann, *et al.* The skilled artisan would have been motivated to do so to detect specific nucleic acid sequences of the isolated cells as taught by Brinchmann, *et al.* There would have been a reasonable expectation of success, given the success of Brinchmann's group. Thus, the invention of claims 18-21 was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

8. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart W. Snyder whose telephone number is (571) 272-9945. The examiner can normally be reached on 9:00 AM-5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Stuart W Snyder
Examiner
Art Unit 1648

SWS



MARY E. MOSHER, PH.D.
PRIMARY EXAMINER